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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/623,761	07/21/2003	John H. Laragh	55990/8	4847
31013      7590      06/04/2009 KRAMER LEVIN NAFTALIS & FRANKEL LLP INTELLECTUAL PROPERTY DEPARTMENT 1177 AVENUE OF THE AMERICAS NEW YORK, NY 10036				
EXAMINER				
SHEN, BIN				
ART UNIT		PAPER NUMBER		
1657				
NOTIFICATION DATE		DELIVERY MODE		
06/04/2009		ELECTRONIC		

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

klpatent@kramerlevin.com

**Office Action Summary****Application No.**

10/623,761

**Applicant(s)**

LARAGH, JOHN H.

**Examiner**

BIN SHEN

**Art Unit**

1657

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 13 May 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 30-33 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 30-33 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SE/US)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

### ***Status of the Claims***

Claims 1-29 are cancelled. Claims 30-33 are presented for examination on the merits.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 30-33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 30, 31 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: what happens if BP is controlled in step B? No need to use a V drug? what happens if BP is controlled with a low dose of a V drug after step C? No need to increase dose of the V drug? more importantly, what happens if BP is not controlled after step D? Administering addition drug?

Claims 30 and 31 are rejected under 35 U.S.C. 112, second paragraph, as using a period after each steps (such as A, B, C, D). This is unacceptable because the only period that you can have in a claim is at the end of the claim.

Claims 32 and 33 are rejected because they depend from cancelled claims.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 30-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands*" 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir., 1988). The court in *Wands* states

"Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' Clearly, enablement of a claimed invention cannot be predicted on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations". The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In the instant case, the specification does not provide any specific guidance on how to treat a hypertensive subject. The closest support provided in the specification is Fig. 4 and 5 however, no example is provided, no discussion about if the method can be used to treat subject already on an R/V drug. Since the specification fails to provide sufficient guidance on how to treat a hypertensive subject having a normal to above/below normal plasma rennin activity, it is necessary to have additional guidance to carry out further experimentation to find out how to make/use the invention. Without more guidance from the specification it would require undue and excessive experimentation for a person having skill in the art to be able to treat hypertensive subject based on plasma rennin activity Since the specification has not described how to treat a hypertensive subject, no direction or guidance presented, no working examples presented, the invention is highly unpredictable regarding the outcome. Thus, claims 30-33 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The

claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

When the factors are considered in their entirety, the Wands analysis dictates a finding of undue experimentation and thus, the claims are not enabled.

applied ).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Louis, McMahon (1978) in view of Laragh (1998)..

Louis teaches a method of treating resistant hypertensive patients with combination of drugs (labetalol, and cyclopentiazide, etc., see page 604, left column, 3rd full paragraph, lines 11-13) and monitoring by measuring BP (page 606, Table 3) and plasma rennin activity level (page 605, Table 2) without discontinue use of the drugs. Therefore, Louis teaches a method of treating a hypertensive subject having a normal to below normal plasma rennin activity level (page 605, Table 2, Basal) by administering to the subject with a low dose of labetalol, and then an increased dose of labetalol if the BP is not controlled (page 604, left column, 3<sup>rd</sup> full paragraph), a low dose of a second drug is administered if the BP is not controlled (diuretic therapy, page 604, left column, 3rd full paragraph, lines 11-14). There is no discontinues use (every few minutes following the administration of labetalol) of the drug prior to measuring plasma rennin activity level (page 605, right column, 1<sup>st</sup> full paragraph, lines 2-7, and Table 2).

**Comment [K1]:** I would make Louis art of record and state that L. teaches to give Lab (R drug) in increasing doses and gives a single dose of diuretic. Go with the 11/21 since they did nothing and there is no reason to give these escalating doses, no discussion of what happens if the patient is already on an R drug, etc. I wanted to keep Louis as 102 baseline. During the interview with the attorney, he suggested the invention is administration of the washout period, and focus exhibit every they had no washout period between two measuring PRA's, as to 11/21: See Fig. 4, doesn't what happens if the BP is controlled in each step, thus I think no 312(c), WDG rejection, and there is still small steps (312/2) in claim 30-33. no 3, can keep L as 102. Tim, you are asserting the claim, not responding to the interview with the attorney 4/26/99

Louis does not teach treating a hypertensive subject with a increased dose of the V drug, having a normal to above normal plasma rennin activity, and the normal level of plasma renin activity is 0.65 ng/ml/h.

McMahon teaches that some clinics routinely test patients for plasma renin activity, and that these patients fall into three categories: low, medium, and high renin activity hypertensive patients. McMahon teaches that low renin patients can be administered a diuretic alone, i.e., a plasma volume-changing drug. Patients with higher plasma renin activity can be administered renin-blocking or -reducing drugs (see p. 3, for example). McMahon also teaches that it is standard practice, when one drug does not appear to be working, to add a second drug of a different type, i.e. if a diuretic is not working, add a renin-blocking agent, for example (see p. 4, for example). Lastly, McMahon teaches that one should treat the hypertension, not the renin level: because hypertension is a disease of high blood pressure, one must inherently monitor the blood pressure. McMahon also teaches that it is standard practice in treating hypertensive patients to titrate the drug to a proper dosage to eliminate the hypertension; determining proper dosage inherently involves measuring the blood pressure response to a given dosage.

Laragh teaches exactly a normal plasma rennin level of 0.65 ng/ml/hr as a guide for diagnosing primary aldosteronism (see p. 171S, col. 2, for example). Laragh teaches that finding a baseline plasma renin activity for every new patient greatly facilitates drug choice. The goal is to find the primary pressor mechanism: high renin indicates an anti-renin drug, while low renin indicates an antivolume drug. Laragh further teaches that the PRA test guides, simplifies, and hastens the selection of the right single drug for each patient (see p. 171 S, col. 2, for example).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of Louis to treat a hypertensive subject having above as well as below normal plasma rennin activity by monitoring drug administration with BP and measuring plasma rennin activity level without the discontinuance use of at least one anti-hypertensive drug because McMahon teaches that patients with medium to high PRA should be prescribed an anti-renin drug to treat the hypertension, and alternatively patients with low PRA should be administered diuretic drugs, and that it is standard practice to titrate dosage to achieve optimal amelioration of hypertensive symptoms (it is inherent that blood pressure should be monitored

because hypertension is a disease of high blood pressure), and Laragh teaches exactly a normal plasma rennin level of 0.65 ng/ml/hr as a guide.. One would have been motivated to make the modification because Louis specifically teaches measuring of PRA concurrently with the administration of the drug (combination of drug) treatment (page 604, left column, line 15), and would reasonably have expected success in view of McMahon teaching of treating patients based on their PRA (low or high) and and Laragh's teaching of a normal rennin level of 0.65 ng/ml/hr. Hence, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to prescribe a renin-blocking drug above 0.65 ng/ml/h PRA, and to modulate dosages (without require the subject to discontinue use of at least one drug) based on blood pressure response to drug administration.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was primafacie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

### ***Conclusion***

No claim is allowed.

Certain papers related to this application may be submitted to Art Unit 1657 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Any inquiry concerning rejections or objections in this communication or earlier communications from the examiner should be directed to Bin Shen, whose telephone number is (571) 272-9040. The examiner can normally be reached on Monday through Friday, from about 9:00 AM to about 5:30 PM. A phone message left at this number will be responded to as soon as possible (i.e., shortly after the examiner returns to her office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon Weber can be reached at (571) 272-0925.

*B. Shen*

Art Unit 1657

/Karen Cochrane Carlson/

Primary Examiner, Art Unit 1656